Attorney's Docket No. US-146O

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
IMAIZUMI et al.	Art Unit: 1652
Application No.: 10/023,711	Examiner: Christian L. FRONDA
Filing Date: December 21, 2001	Attorney Ref. No.: US-146O
For: METHOD OF PRODUCING TARGET SUBSTANCE BY FERMENTATION	Confirmation No.: 6895

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
Alexandria, Virginia 22313

Sir:

In response to the Non-Final Office Action dated March 4, 2009, the response period being extended by a one-month extension of time and a Notice of Appeal filed herewith, to July 4, 2009, Applicants request a Pre-Appeal Brief Review in accordance with the guidelines set forth in the July 12, 2005 Official Gazette Notice. Reconsideration of this application by a three Examiner panel is requested in view of the following remarks which identify the errors in facts, and the omission of essential elements required to establish a *prima facie* rejection.

Summary of Final Office Action and Status of Case

In the non-final Office Action mailed March 4, 2009, Claims 7, 8, 12 and 13 stand rejected under 35 U.S.C. §112, 1st paragraph, as allegedly the specification does not provide enablement for the claimed invention, in that it is alleged that the strains WC196Δrmf and WC196Δrmf/pMP1700 are required to practice the invention, are not adequately described, and hence must be deposited. The claims were previously rejected under this statute and for this same reason in the Office Action issued December 5, 2005. This rejection was successfully overcome as indicated in the Office Action of August 10, 2006 in response to Applicant's arguments and exhibits filed May 5, 2006. As the claims have been rejected at

least twice under this section, this appeal and this pre-appeal request are timely filed. Claims 1, 6, 9-11, and 14 are allowable. Claims 2-5 were cancelled.

Summary of Claimed Invention

The claimed invention is directed to a method for producing an L-amino acid comprising culturing an *Escherichia coli* bacterium in a medium, allowing said L-amino acid to accumulate in the medium and/or in the cells of the bacterium, and collecting said L-amino acid, wherein the endogenous *Escherichia coli* gene encoding the RMF protein is mutated so that the RMF protein is inactive, and wherein said L-amino acid is produced in larger quantities than if the RMF protein were active.

Factual Errors Requiring Review

The claims stand rejected on the grounds that the specification is allegedly only enabling under 35 U.S.C. §112, 1st paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully requests reconsideration of this rejection.

The Examiner is requiring a deposit of the WC196Δrmf and WC196Δrmf/pMP1700 strains. It is alleged that the process disclosed in the specification to make these strains does not appear to be repeatable because the nucleotide sequences of the plasmid vectors used to transform the parent strains are not fully disclosed. The Office Action further alleges that "nor have all the nucleotide sequences required for their construction been shown to be biblically known and freely available." Finally, the Office Action alleges "it is not apparent that the source materials to make the WC196Δrmf 196 and WC196Δrmf/pMP1700 strains are both known and readily available to the public."

First, the requirement for a deposit is a clear error since this rejection and deposit requirement was made in the Office Action of December 5, 2005, successfully argued in the response filed May 5, 2006, and withdrawn by this same Examiner in the Office Action of August 10, 2006. This is a clear error because the new deposit requirement set forth in this most recent Office Action mailed March 4, 2009 repeats the same rejection, but provides no new arguments, bases, or explanations in addition to those made in December 2005. In fact, it appears that the previous rejection has merely been repeated, with no explanation as to why it was previously made and withdrawn, and now is being made again. Secondly, it is unclear as to exactly what is meant by the requirement that the nucleotide sequences be "biblically known

and freely available". One of ordinary skill in the art only needs to be able to make and use the invention as it is described in the specification in light of that known in the prior art, and clearly with the wealth of information in the prior art concerning the *rmf* gene and that provided in the specification, the claimed invention is clearly adequately enabled and described. No deposit is necessary, as the strains can be made according to the description in the specification and the wealth of information in the prior art, including the previously described and deposited source materials.

The basis and reasons for the rejection remain in error, and the statements made in the Office Action of March 4, 2009 are incorrect, but will be addressed again, and in a similar manner as to how they were successfully addressed in the response filed May 5, 2006. The WC196Δrmf strain can be prepared from the deposited strain WC196 (AJ13069) according to the description in the specification (see Example 2) and in light of that which was known in the art. Therefore, since the WC196Δrmf strain was readily obtainable by the methods set forth in the specification combined with the knowledge in the art, a deposit of the strains is unnecessary. Furthermore, the WC196Δrmf/pMP1700 can be made from the WC196Δrmf strain by the methods shown in the specification (see Example 3), and hence is also readily obtainable using the description in the specification and known methods in the art, and therefore, a deposit of this strain is also unnecessary. Therefore, the source materials necessary to make the WC196Δrmf and WC196Δrmf/pMP1700 strains are known and readily available.

The claimed invention requires that the known *rmf* gene is mutated so that the RMF protein is inactivated. As shown in the Exhibits that were filed with the response of May 5, 2006, the nucleotide sequence of the *rmf* gene and the crossover PCR method used to disrupt this gene as shown in example 2 in the specification have been known since well before the priority date of the application. The Link et al. article (Exhibit C in the response filed May 5, 2006) clearly shows the use of cross-over PCR for disruption of the *E.coli* genome by crossover PCR, and that such techniques were well-known in the art. As for the assertion in the Office Action that the specification does not disclose the specific nucleotide sequence of the inactivated *rmf* gene, applicants assert that the specification does disclose the sequences of the four primers and the methods for obtaining an inactivated gene. The prior art (see Yamagishi et al., *EMBO J.* (1993) 12:625-630, cited in the specification by applicants and throughout prosecution by the Examiner) describes the entire sequence of the *rmf* gene.

Clearly such knowledge in the prior art combined with the primer sequences in the specification, provides a clear description of the inactivated gene since one of skill in the art could easily determine the complementary regions based up on the primers, and determine the structure of the inactivated gene following the well-known prior technique of cross-over PCR.

Again, no new arguments or bases for this rejection have been advanced since this rejection was initially made and overcome 3 years ago. Therefore, the rejection is in clear error and must be withdrawn. For at least the foregoing reasons, Applicant respectfully submits that Claims 7, 8, 12 and 13 fully comply with 35 U.S.C. § 112, first paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

Conclusion

In the interest of brevity, Applicant does not provide all arguments that would support an appeal for each of the pending and rejected claims. However, it is respectfully submitted that this case is in immediate and clear form for allowance based on the clear errors and omissions cited above. Accordingly, an early indication via a Notice of Allowability that all claims are allowable is respectfully requested. Should any questions arise in connection with this application or should the Examiner believe that a telephone conference with the undersigned would be helpful in resolving any remaining issues pertaining to this application, the undersigned respectfully requests that he be contacted at the number indicated below.

Respectfully submitted,

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